Epilepsy and Developmental Disabilities

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Objectives:

1. Identify effective methods for the practical application of concepts related to improving the delivery of services for persons with developmental disabilities

2. Identify advances in clinical assessment and management of selected healthcare issues related to persons with developmental disabilities

3. Identify and emphasize attitudes that enhance the opportunities for persons with DD to achieve their optimal potential

Notes:
Epilepsy in the Developmentally Disabled

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Disclosures

• Speaker has no disclosures to make
• Some medication options may be off-label (to be specified)
Spectrum of developmental disabilities

- Cognitive impairment
- Cerebral palsy
- Autism spectrum disorders

Associations

- 15-35% of epilepsy with onset in childhood associated with cognitive impairment, CP
- Epilepsy is the most common co-morbidity with developmental disabilities
- Higher degree of impairment, higher likelihood of seizures
- Underlying cause of CI and seizures the same
- > 50% of institutionalized patients have epilepsy (compared to <1% of gen population)
IQ and seizures

Table 5-2: Occurrence of Epilepsy Among Various Intellectual Categories

<table>
<thead>
<tr>
<th>Intellectual Category</th>
<th>Prevalence of Epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal IQ</td>
<td>1%</td>
</tr>
<tr>
<td>Mild mental retardation (IQ 50–70)</td>
<td>15%</td>
</tr>
<tr>
<td>Severe mental retardation (IQ &lt; 50)</td>
<td>47%</td>
</tr>
</tbody>
</table>


Seizures & Cerebral Palsy

- Seizure risk higher in spastic quadriparesis (50-94%) and hemiparetic CP (30%)
- Less common in dystonic CP
- Least common in spastic diplegic CP
- >50% when there is combination of cognitive impairment and CP

Comorbid Neurolgic Handicaps

Table 5-3: Associations of Comorbid Neurolgic Handicaps in Children from the National Collaborative Perinatal Project (NCP)

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>CP</th>
<th>SI</th>
<th>MMR</th>
<th>SMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP</td>
<td>33.9%</td>
<td>30%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>CP and MR</td>
<td>35%</td>
<td>35%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>27%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quadraplegia</td>
<td>73%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF</td>
<td>27%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MR</td>
<td>20%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral Palsy</td>
<td>20%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td>27%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMR</td>
<td>20%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autism</td>
<td>20%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CP = cerebral palsy; SI = seizures; MMR = mild mental retardation; SMR = severe mental retardation; MR = mental retardation. All independent variables are listed in the leftmost column. (2013 WUA).
IQ and seizure type

Figure 16-6. Frequency distribution of IQ scores among children with various seizure types. The percentage values shown in parentheses indicate the proportion of the group that is expected to have an IQ of 79 or less. The average and standard deviations (SD) for the groups are as follows: Absence (IQ 100.7, SD 14.6); mixed (IQ 94.3, SD 22.7), and generalized absence (IQ 109.7, SD 16.4).

IQ Distribution

Figure 16-3. IQ distributions for people affected by disorders associated with epilepsy. (Developed from information in Elements of Mental Retardation, Ashkenazi, M., Kennedy, W. A. Preschool IQ: Memory and Early Developmental Correlates. Hillsdale, N.J.: Lawrence Erlbaum Associates, Publishers, 1975.)

IQ and seizure frequency

Figure 16-5. Effect of seizure frequency on full-scale IQ among people having seizure frequencies that were 1 low 1 or fewer seizures per year, moderate 1 12 seizures per year, or high 12 or more seizures per year. Adapted from Ekren S, Mathews CG. Harley P., Effect of early versus late onset of major motor epilepsy on cognitive/intellectual performance: Further considerations. Epilepsia 1977; 18:33-36.
IQ Distribution in Epileptic Children

Seizures & Autism

• Greater the degree of cognitive impairment, greater the risk of epilepsy
• Estimates range from 8-30% overall

Types of seizures seen

• Generalized tonic clonic  42%
• Myoclonic
• Atypical absence
• Complex partial

• Nearly ½ have more than 1 seizure type
• Approximately 40% have seizure at least weekly
Overall

• Multiple seizure types
• Seizures in developmentally disabled are more likely refractory to current treatments
• Cluster seizures are more likely
• Status epilepticus more likely
• Medical complications and injury more likely

Likelihood of seizure control lowest with

• Greater degree of disability
• Multiple co-existing disabilities
• Multiple seizure type
• Known underlying brain lesion or disorder
• Multi-focal epileptiform discharges
• When multiple medications are needed
Limitations of diagnosis

• Individuals may be non-verbal
• May be institutionalized
• May have episodes or movements which can be mistaken for seizures
• Subtle seizures which may blend in with individual’s behavior

Difficulties in making a diagnosis

• Individuals may be non-verbal or not fluent
• History may be have to be obtained from caregivers who may have many individuals to take care of and may have variable training
• May be difficult to diagnose subtle seizures and to differentiate from non-epileptic events
• May be difficult is some cases to get EEGs
• Sedation or anesthesia may be required to accomplish test such as MRI or CT

Multi-disciplinary treatment team with input from:

• Direct care staff
• Primary care physician
• Nursing staff
• Occupational and physical therapists
• Educational specialists, teachers
• Speech and language therapists
• Social workers
• The family
Behaviors which may mimic seizures

- Abnormal movements such as tics, tremors, dystonia, chorea
- Staring
- Compulsions
- Stereotypic behaviors
- Sleep disorders
- Gastroesophageal reflux
- Self-injurious behaviors
- Aggression
- Sudden outbursts
- Tonic posturing

Seizure triggers unique to developmentally disabled

- Irregular sleep patterns and sleep deprivation
- Emotional stress: change in caretaker, change in routines
- Menstrual cycles
- Infections: examples are aspiration, urinary tract infections
- Electrolyte disturbances: from compulsive water drinking

Principles of treatment

- Monotherapy preferable in many cases
- Broad spectrum seizure medication for multiple seizure types
- Minimize potential drug interactions
- Minimize adverse effects particularly cognitive and sedative
- Start and increase slowly if possible
- Avoid exacerbating co-morbid conditions
- Try once a day or twice a day doses
- Simplify medication regimen
- Focus on quality of life besides seizure freedom
Why a single drug is better

• Better efficacy most times
• Better compliance
• Less interactions between drugs
• Less toxicity
• Easy to manage
• Less expensive
  — But sometimes you don’t have a choice and you have to treat with more than one medication

Response to Seizure Medication:
5-Year Follow-Up

• 525 newly diagnosed patients (adults and kids)
  — 470 AED-naïve
  — 55 AED-experienced
• 63% seizure-free for 1 year
  — AED-naïve: 64%
  — 60% after first or second monotherapy trial
  — AED-experienced: 56%
• Most withdrawals or change of treatment were due to intolerable side effects

Simplify medication regimen if possible

- Try to wean old drug after new one introduced
- Try once or twice a day dose
- Multiple medications can be given at same time

Broad-spectrum seizure medications: Clinical Implications

The ideal anticonvulsant?
Broad spectrum seizure medications

- Valproic acid, sodium valproate
- Topiramate
- Zonisamide
- Lamotrigine
- (Levetiracetam)
- (Felbamate)
- (Rufinamide)

Drugs for partial onset seizures

- Carbamazepine
- Oxcarbazepine
- Phenytoin
- Tiagabine
- Gabapentin
- Phenobarbital
- Lamotrigine

Medications with possible sedative side effects

- Phenobarbital, primidone
- Benzodiazepines: clonazepam, clorazepate, clobazam
- Any seizure medication can cause sedative side effects but the above are more likely to do so
Seizure medication side effects unique to developmentally disabled

- **Weight loss**: Topiramate, Zonisamide, Felbamate
- **Weight gain**: Valproic acid, Gabapentin
- **Kidney stones**: Topiramate, Zonisamide
- **Cognitive/sedative/behavior effects**: all
- **Vitamin D Bone health effects**: (cytochrome p450) enzyme inducing anticonvulsants
- **Cosmetic**: phenytoin

Seizure medications with possible long-term side effects

- Cytochrome p450 enzyme inducing drugs: **bone density loss**
- Phenytoin: coarsening of facial features, gum swelling, hirsutism, peripheral neuropathy, cerebellar atrophy
- Valproic acid: hair loss, weight gain
- Phenobarbital, primidone, phenytoin: connective tissue disorders such as Dupuytren's contractures

Why developmentally disabled are prone to bone loss

- Suboptimal nutrition
- High metabolic needs
- Impaired mobility and weight bearing
- May be on medications which increase calcium turnover
Monitoring for bone loss with enzyme inducing seizure medications

- Drugs: phenobarbital, phenytoin, carbamazepine
- Check: vitamin D (25 hydroxy-vitamin D level)
- Give vitamin D and supplemental calcium

- No good studies yet looking at this association long-term

Compliance and Seizure Control

- 661 patients taking AEDs
  - National survey
  - 71% of patients missed at least 1 dose
    - Mean of 1.99 missed doses/month
- Odds of experiencing a seizure following a missed dose were highest among those taking:
  - A greater number of pills/day
  - More frequent dosing: qid>tid>bid>qd

Impact of Dosing Frequency on Compliance

- In epilepsy patients
  - Higher compliance rates are associated with once-daily dosing
- Noncompliance with AEDs is a major factor in:
  - Breakthrough seizures
  - Recurrence of seizures
Peak = Toxicity

Trough = Efficacy

Immediate Release

Sustained Release

Area under the curve the same for both (AUC)

Higher troughs and lower peaks for sustained release

Simulated Pharmacokinetics: Once-Daily, Extended-Release

Day 1

Peak: Side Effects

Day 2

Zone of Seizure Control

Concentration

Time (h)

0 8 16 24 32 40 48
Special consideration in developmentally disabled

• Absorption rates may be faster
• Metabolic rates may be faster
• Protein binding may be lower
• Clearance may be higher
• May not be able to swallow tablets
• Certain adverse effects may be higher
• Medications may have to be given through a gastrostomy

AED Delivery Systems for Developmentally Disabled: Options to Simplify Therapy

• Extended-release
• Suspension
• Syrup
• Sprinkle capsules
• Chewable tablets
• Dispersible tablets
• Sublingual
• IV/IM
• Rectal

Status epilepticus or seizure clusters

(some of these are off label)

• Rectal diazepam
• Clonazepam (Klonopin) oral
• Lorazepam (Ativan) oral, sublingual
• Midazolam (Versed) intranasally
• IV or IM fosphenytoin
• Levetiracetam (Keppra) oral
• IV Lacosamide (Vimpat)
Diastat (Diazepam) Rectal gel

- Pre-hospital (can be used in hospital also) treatment of status epilepticus
- seizure clusters
- febrile seizures
- safe for administration by parent
- lipid soluble, crosses into CNS
- somnolence, but no respiratory depression
- 0.2-0.5mg/kg, pre-filled syringes
Dose-concentration for IV and rectal diazepam

Types of adverse effects

- **Dose related**
  - Somnolence
  - Irritability
  - Behavior changes
  - Cognitive
  - Asthenia
  - Dizziness

- **Idiosyncratic**
  - Hepatotoxicity
  - Blood counts
  - Cutaneous
  - Teratogenicity
  - Kidney stones
  - Glaucoma
Overall Quality of Life

Seizure control  Side effects, Particularly affecting alertness, cognitive functioning and mood

Newer medications

- Rufinamide (Banzel)
- Lacosamide (Vimpat)
- Vigabatrin (Sabril)
- Ezogabine (retigabine in Europe) (Potiga)
- (Eslicarbazepine)
- Clobazam (Onfi)

Risk for injury

- Epilepsy is an independent risk factor for injury
- 15% risk for fracture with developmentally disabled
- 25% risk when combined with epilepsy
- May be increased due to poor bone health, abnormal gait or non-ambulatory status